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W P E R L H (TW)

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MPsrch\_pp protein - protein database search, using Smith-Waterman algorithm

Run on: Mon Oct 2 09:33:11 2000; MasPar time 6.68 Seconds  
Tabular output not generated. 436.063 Million cell updates/sec

Title: >US-09-381-497-2  
Description: (1-123) from US09381497.pep  
Perfect Score: 903  
Sequence: 1 EVOLVESGGLVKPGSLKL.....SSYGVLFAWGQGLTVTUSA 123  
Scoring table: PAM 150  
Gap 11

Searched: 188963 seqs, 23686106 residues

Post-processing: Minimum Match 0%  
Listing first 45 summaries

Database: a-geneseq36  
1:geneseqp

Statistics: Mean 30.324; Variance 152.652; scale 0.199

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

SUMMARIES

Result No.	Score	Query Match %	Length	ID	Description	Pred. No.
1	896	99.2	123	1	W66099 anti-CD22 monoclonal a	1.58e-63
2	748	82.8	121	1	W86125 protein sequence of mo	3.76e-51
3	744	82.4	121	1	W22951 Monoclonal antibody (M	8.11e-51
4	744	82.4	121	1	W86118 Murine 340 VH amino ac	8.11e-51
5	735	81.4	139	1	W21656 Chimeric MAB 15 PCR-mo	4.56e-50
6	730	80.8	140	1	W21654 Mouse MAB 15 heavy cha	1.19e-49
7	728	80.6	136	1	R06251 Variable region of mur	1.75e-49
8	717	79.4	139	1	R52773 Murine KC-4 immunoglob	1.44e-48
9	717	79.4	139	1	R52791 Murine KC-4 immunoglob	1.44e-48
10	716	79.3	118	1	W89627 Mouse humanised antibo	1.74e-48
11	716	79.3	118	1	W57576 Chimeric H chain SEQ I	1.74e-48
12	716	79.3	137	1	W89625 Mouse humanised antibo	1.74e-48
13	716	79.3	137	1	W57592 Chimeric antibody agai	1.74e-48
14	716	79.3	247	1	W11917 Murine MAB SK48-E26 he	1.74e-48
15	713	79.0	121	1	W86122 Protein sequence of de	3.10e-48
16	713	79.0	123	1	W08582 Human antibody C4.1 he	3.10e-48
17	712	78.8	121	1	W86120 Protein sequence of hu	3.75e-48
18	712	78.8	139	1	W21652 Humanised reshaped MAB	3.75e-48
19	710	78.6	138	1	R20064 MRK16-H chain.	5.50e-48
20	709	78.5	117	1	R76003 LM609 antibody heavy c	6.67e-48
21	706	78.2	142	1	R30882 Antibody 4A2 heavy cha	1.18e-47
22	704	78.0	138	1	W03722 Anti-human gp39 MAB 39	1.74e-47
23	703	77.9	123	1	R43827 Anti-lysozyme VH.	2.10e-47

24	703	77.9	123	1	R45187 Heavy chain variable d	2.10e-47
25	700	77.5	119	1	W35503 Antibody 15D3 heavy ch	3.74e-47
26	700	77.5	119	1	W69322 15D3 antibody heavy ch	3.74e-47
27	700	77.5	158	1	W19577 Mouse anti-idiotypic a	3.74e-47
28	700	77.5	158	1	W19579 Mouse anti-idiotypic a	3.74e-47
29	698	77.3	119	1	W29996 Humanised variant of h	5.48e-47
30	697	77.2	120	1	W00240 EGF receptor chimeric	6.64e-47
31	696	77.1	117	1	R79155 Human IgE receptor-bln	8.04e-47
32	696	77.1	117	1	W27354 Heavy chain variable r	8.04e-47
33	696	77.1	117	1	W27357 Heavy chain variable r	8.04e-47
34	693	76.7	121	1	W86124 Protein sequence of al	1.43e-46
35	692	76.6	118	1	R41233 Monoclonal antibody BW	1.73e-46
36	692	76.6	119	1	R56239 VH region of anti-fuco	1.73e-46
37	692	76.6	138	1	R32246 BR55-2 murine IgG3 hea	1.73e-46
38	692	76.6	138	1	R32242 Chimeric MAB heavy cha	1.73e-46
39	692	76.6	139	1	R31588 BR55-2 heavy chain var	1.73e-46
40	691	76.5	119	1	W29994 Heavy chain variable r	2.09e-46
41	691	76.5	140	1	W05205 Xenograft antibody HAR	2.09e-46
42	689	76.3	448	1	R97376 Murine anti-BGH MAB he	3.07e-46
43	687	76.1	448	1	R43673 Mouse anti-bovine grow	4.50e-46
44	686	76.0	448	1	R06476 Heavy chain of anti-bo	5.45e-46
45	685	75.9	117	1	R79157 Human IgE receptor-bln	6.60e-46

ALIGNMENTS

RESULT 1  
ID W66099 standard; Protein; 123 AA.  
AC W66099;  
DT 10-DEC-1998 (first entry)  
DE anti-CD22 monoclonal antibody heavy chain variable region.  
KW anti-CD22 monoclonal antibody heavy chain variable region; VL;  
KW Pseudomonas exotoxin; variable heavy chain; VH; variable light chain;  
OS Mammalia.  
FH Key Location/Qualifiers  
FT Misc\_difference 121 /note= "Encoded by gtc"  
PN WO9841641-A1.  
PD 24-SEP-1998.  
PF 19-MAR-1998; U05453.  
PR 20-MAR-1997; US-041437.  
PA (USSH ) US DEPT HEALTH & HUMAN SERVICES.  
PI Fitzgerald D, Kreitman R, Mansfield E, Pastan I;  
DR WPI: 98-521227-44.  
DR N-PSDB: V07642.  
PT Recombinant anti-CD22 antibodies and immuno-conjugates - of  
PT antibodies linked to a therapeutic agent, e.g. Pseudomonas exotoxin  
or a label; for inhibiting malignant B-cells  
PS Claim 6; Fig 1; 71pp; English.  
CC The invention claims for a recombinant immunoconjugate comprising  
of a therapeutic agent (e.g. Pseudomonas exotoxin) or a detectable  
label peptide bonded to a recombinant anti-CD22 antibody (RFB4 IgG)  
having the present variable heavy (VH) chain with a cysteine residue  
at amino acid 44 and a variable light (VL; W66098) chain with a  
cysteine residue at amino acid 100. The immunoconjugate is claimed  
to inhibit the growth of malignant B-cells in vivo, such as rodent,  
canine or primate B-cells. The anti-CD22 antibody is claimed useful  
for detecting CD22 protein in a sample or in vivo in a mammal, and  
can be used in diagnostic kits.  
SQ Sequence 123 AA;

Query Match 99.2%; Score 896; DB 1; Length 123;  
Best Local Similarity 99.2%; Pred. No. 1.58e-63;  
Matches 122; Conservative 0; Mismatches 1; Indels 0; Gaps 0;

Db	1	EVOLVESGGLVKPGSLKLSCAASGFAFSIYDMSVWROTPEKRLWEWAYISSGGGTTY 60
Qy	1	EVOLVESGGLVKPGSLKLSCAASGFAFSIYDMSVWROTPEKRLWEWAYISSGGGTTY 60
Db	61	PDTVKGRFTISRDNAKNTLYLQMSLKSEDYAMYYCARHSGYSSGYVLFAWGQGLTVT 120
Qy	61	PDTVKGRFTISRDNAKNTLYLQMSLKSEDYAMYYCARHSGYSSGYVLFAWGQGLTVT 120



PD 26-NOV-1998.  
 PF 21-MAY-1998; G01473.  
 PR 14-APR-1998; GB-007751.  
 PR 21-MAY-1997; GB-010480.  
 PR 31-JUL-1997; GB-016197.  
 PR 28-NOV-1997; GB-025270.  
 PR 02-DEC-1997; US-067235.  
 PA (BIOV-) BIOVATION LTD.  
 PI Carr FJ;  
 DR WPI; 99-045301/04.  
 DR N-PSDB; V81002.  
 PT Reducing immunogenicity of proteins - by modifying the amino acid  
 PT sequence of the protein to eliminate potential epitopes for T-cells  
 PT of a given species  
 PS Example 1; Fig 2; 77pp; English.  
 CC The invention relates to a method for the production of non-immunogenic  
 CC proteins. The method comprises determining at least part of the amino  
 CC acid sequence of the protein; (b) identifying in the amino acid sequence  
 CC one or more potential epitopes for T-cells (T-cell epitopes) of the given  
 CC species; and (c) modifying the amino acid sequence to eliminate at least  
 CC one of the T-cell epitopes identified in step (b) thereby to eliminate or  
 CC reduce the immunogenicity of the protein when exposed to the immune  
 CC system-of-the-given-species. A method of analysing a pre-existing protein  
 CC to predict the basis for immunogenic responses is also provided. The  
 CC methods can be used particularly for reducing the immunogenicity of  
 CC immunoglobulins or therapeutic proteins, e.g. Streptokinase (SK). The  
 CC products can be used for diagnosis and therapy. The present sequence  
 CC represents the amino acid sequence of murine 340 Vh.  
 SQ Sequence 121 AA;

Query Match 82.4%; Score 744; DB 1; Length 121;  
 Best Local Similarity 83.7%; Pred. No. 8,11e-51;  
 Matches 103; Conservative 7; Mismatches 11; Indels 2; Gaps 1;

Db 1 EVQLVESGGGLVKGAGSLKLSCAASGFAFDYDMSWVROTPEKRLWVAYIGSGGRTYY 60  
 QY 1 EVQLVESGGGLVKGAGSLKLSCAASGFAFDYDMSWVROTPEKRLWVAYISGGGTTY 60

Db 61 PDTVKGRTISRDNKNTLYLQNSLKSEDTAMYYCARHGHVYDVA--DYWGQGTSTV 118  
 QY 61 PDTVKGRTISRDNKNTLYLQNSLKSEDTAMYYCARHGHVYDVA--DYWGQGTSTV 118

Db 119 VSS 121  
 QY 121 VSA 123

RESULT 5  
 ID W21656 standard; Protein; 139 AA.

AC W21656;  
 DT 03-JAN-1998 (first entry)  
 DE Chimeric MAB 15 PCR-modified heavy chain variable region.  
 KW Humanised antibody; monoclonal antibody; MAB 15; tumour;  
 KW lung cancer; therapy.  
 OS Chimeric Mus musculus.  
 OS Chimeric synthetic.

FH Key Location/Qualifiers  
 FT Peptide 1..19  
 FT /label= Sig\_peptide  
 FT Protein 25..139  
 FT /label= Mat\_protein  
 FT Region 20..49  
 FT /label= Framework-1  
 FT Region 50..54  
 FT /label= CDR1  
 FT /note= "complementarity determining region 1"  
 FT Region 55..68  
 FT /label= Framework-2  
 FT Region 69..86  
 FT /label= CDR2  
 FT /note= "complementarity determining region 2"  
 FT Region 87..117  
 FT /label= Framework-3  
 FT /note= "complementarity determining region 3"

FT Region 118..128  
 FT /label= CDR3  
 FT /note= "complementarity determining region 3"  
 FT 129..138  
 FT /label= Framework-4  
 PN EP-781847-A1.  
 PD 02-JUL-1997.  
 PD 25-OCT-1996; 117154.  
 PR 06-NOV-1995; EP-117407.  
 PR (MERE ) MERCK PATENT GMBH.  
 PI Bendig M, Jones T, Saldana J;  
 DR WPI; 97-334904/31.  
 DR N-PSDB; T72269.  
 PT Humanised form of murine monoclonal antibody MAB 15 - useful for  
 PT treating lung cancer  
 PS Disclosure; Fig 5; 71pp; English.  
 CC This polypeptide comprises the heavy chain variable region VH  
 CC region of murine monoclonal antibody (MAB) 15 (DSM ACC2117). It is  
 CC encoded by a MAB 15 VH cDNA sequence (372269) modified for the  
 CC expression of chimeric antibody. The VL sequence was similarly  
 CC obtained (see W21655). The modified VH and VL sequences were used  
 CC in a claimed process to model and design novel humanised, reshaped  
 CC MAB 15 having humanised, reshaped VH and VL sequences (see W21652  
 CC and W21651), which can be used for treating tumours, especially  
 CC lung cancer, and for the manufacture of a drug related to tumours,  
 CC especially lung cancer.  
 SQ Sequence 139 AA;

Query Match 81.4%; Score 735; DB 1; Length 139;  
 Best Local Similarity 82.9%; Pred. No. 4.56e-50;  
 Matches 102; Conservative 9; Mismatches 9; Indels 3; Gaps 1;

Db 20 EVQVESGGGLVKGAGSLKLSCAASGFAFDYDMSWVROTPEKRLWVAYLSRGGSTYY 79  
 QY 1 EVQVESGGGLVKGAGSLKLSCAASGFAFDYDMSWVROTPEKRLWVAYISGGGTTY 60

Db 80 PDTVKGRTISRDNKNTLYLQNSLKSEDTAMYYCARHGHVYDVA--FDYWGQGTSTV 136  
 QY 61 PDTVKGRTISRDNKNTLYLQNSLKSEDTAMYYCARHGHVYDVA--FDYWGQGTSTV 120

Db 137 VSA 139  
 QY 121 VSA 123

RESULT 6  
 ID W21654 standard; Protein; 140 AA.

AC W21654;  
 DT 03-JAN-1998 (first entry)  
 DE Mouse MAB 15 heavy chain variable region.  
 KW Humanised antibody; monoclonal antibody; MAB 15; tumour;  
 KW lung cancer; therapy.  
 OS Mus musculus.

FH Key Location/Qualifiers  
 FT Peptide 1..19  
 FT /label= Sig\_peptide  
 FT Protein 20..140  
 FT /label= Mat\_protein  
 FT Region 20..49  
 FT /label= Framework-1  
 FT Region 50..53  
 FT /label= CDR1  
 FT /note= "complementarity determining region 1"  
 FT Region 54..68  
 FT /label= Framework-2  
 FT Region 69..86  
 FT /label= CDR2  
 FT /note= "complementarity determining region 2"  
 FT Region 87..117  
 FT /label= Framework-3  
 FT /label= CDR3  
 FT /note= "complementarity determining region 3"

```
FT Region 129..139
FT /label= Framework-4
PN EP-781847-A1.
PD 02-JUL-1997.
PP 25-OCT-1996; 117154.
PR 06-NOV-1995; EP-117407.
PA (MERE ) MERCK PATENT GMBH.
PI Bendig M, Jones T, Saldana J;
DR N-PSDB; T72267.
DR Humanised form of murine monoclonal antibody MAB 15 - useful for
PT treating lung cancer
PT Example 1; Fig 2; 71pp; English.
PS This polypeptide comprises the heavy chain variable region VH
CC of murine monoclonal antibody (MAB) 15 (DSM ACC2117), a MAB that
CC shows a therapeutic effect on human tumour cells, especially human
CC lung cancer. Its sequence was deduced from an isolated cDNA
CC cloner (see T72267). The MAB 15 VL region sequence (W21653)
CC has also been determined. Amplified VH and VL cDNA sequences were
CC used in a claimed process for the production of novel humanised,
CC reshaped MAB 15 having humanised, reshaped VH and VL regions (see
CC W21652 and W21651), which can be used for treating tumours,
CC especially lung cancer, and for the manufacture of a drug related
CC to tumours, especially lung cancer.
SQ Sequence 140 AA;

Query Match 80.8%; Score 730; DB 1; Length 140;
Best Local Similarity 82.1%; Pred. No. 1.19e-49;
Matches 101; Conservative 10; Mismatches 9; Indels 3; Gaps 1;

Db 20 EVQVSEGGGLVPGGSLKLSCAASGFAFSYDMSWVRQTPKRLWVAYISSGGTTY 79
QY 1 EVQVSEGGGLVPGGSLKLSCAASGFAFSYDMSWVRQTPKRLWVAYISSGGTTY 60

Db 80 PDTVKGRFTISRDNKNTLYLQMSLSKASEDTAMTYCARHSGYGVLFAYWGQGLT 136
QY 61 PDTVKGRFTISRDNKNTLYLQMSLSKASEDTAMTYCARHSGYGVLFAYWGQGLT 120

Db 137 VSA 139
QY 121 VSA 123

RESULT 7
ID R06251; standard; protein; 136 AA.
AC R06251;
DT 10-DEC-1990--(first-entry)
DE Variable region of murine AHT 54 heavy chain.
KW Interleukin-2 receptor; IL-2; tumour necrosis factor; TNF; ss.
OS Mus sp.
PN EP-380068-A.
PD 01-AUG-1990.
PP 24-JAN-1990; 101351.
PR 24-JAN-1989; US-301216.
PR 04-DEC-1989; US-441702.
PA (MOLE-) MOLECULAR THERAPU.
PI Zarler B;
DR WPI; 90-232892/31.
DR N-PSDB; Q05355.
PT Expression vectors for producing chimeric monoclonal antibodies -
PT which express human constant region and non-human variable region
PS Disclosure; p; English.
CC Mabs comprising mouse CH and CL constant regions which human
CC variable regions may be used to create mouse/human hybrid MABs,
CC which have a longer serum half-life. Method can be used to produce
CC Abs against interleukin-2 receptor and tumour necrosis factor.
SQ Sequence 136 AA;

Query Match 80.6%; Score 728; DB 1; Length 136;
Best Local Similarity 88.6%; Pred. No. 1.75e-49;
Matches 109; Conservative 3; Mismatches 5; Indels 6; Gaps 1;

Db 20 EVQVSEGGGLVPGGSLKLSCAASGFAFSYDMSWVRQTPKRLWVAYISSGGTTY 79
```

```
QY 1 EVQVSEGGGLVPGGSLKLSCAASGFAFSYDMSWVRQTPKRLWVAYISSGGTTY 60
Db 80 PDTVKGRFTISRDNKNTLYLQMSLSKASEDTAMTYCARHSGYGVLFAYWGQGLT 133
QY 61 PDTVKGRFTISRDNKNTLYLQMSLSKASEDTAMTYCARHSGYGVLFAYWGQGLT 120
Db 134 VSA 136
QY 121 VSA 123

RESULT 8
ID R52773; standard; Protein; 139 AA.
AC R52773;
DT 24-JAN-1995 (first entry)
DE Murine KC-4 immunoglobulin heavy chain variable region (deduced).
KW Immunoglobulin variable domain; primer; polymerase chain reaction;
KW chimeric antibody; human milk fat globule; human breast carcinoma;
KW murine anti-human carcinoma monoclonal antibody KC-4.
OS Mus musculus.
FH Key Location/Qualifiers
FT Protein 20..139
FT /label= KC-4_mature_VL-chain
FT region 20..49
FT /label= FR1
FT region 50..54
FT /label= CDR1
FT region 55..68
FT /label= FR2
FT region 69..85
FT /label= CDR2
FT region 86..117
FT /label= FR3
FT region 118..128
FT /label= CDR3
FT region 129..139
FT /label= FR4
PN W09411508-A.
PD 26-MAY-1994.
PP 15-NOV-1993; U11316.
PR 13-NOV-1992; US-977706.
PR 13-NOV-1992; US-977707.
PR 28-SEP-1993; US-128015.
PA (CANC-) CANCER RES FUND CONTRA COSTA.
DR WPI; 94-183509/22.
DR N-PSDB; -Q62764-.
PT Chimeric human-murine polypeptide(s) specific for human mammary
PT fat globule antigen - for imaging, diagnosing and treating
PT neoplasia, with less undesirable immunogenic response
PS Example 27; Page 41; 54pp; English.
CC An initial isolation of cDNAs coding for murine anti-human breast
CC carcinoma MAB KC-4 was performed using PCR with commercially
CC available primers (see Q62751-Q62758, available from NOVAGEN).
CC Subsequent cloning using PCR primers JO20, JO21, JO22 and JO24
CC (see Q62759-Q62762) resulted in the isolation of the mouse Ig
CC variable domains. The amplified cDNAs were sequenced (Q62763 and
CC Q62764) and amino acid sequences were deduced from them. Chimeric
CC mouse-human antibodies were constructed using human constant
CC regions so as to produce less immunogenic polypeptides which
CC retained the anti-human carcinoma binding specificity of KC-4.
SQ Sequence 139 AA;

Query Match 79.4%; Score 717; DB 1; Length 139;
Best Local Similarity 82.1%; Pred. No. 1.44e-48;
Matches 101; Conservative 8; Mismatches 11; Indels 3; Gaps 3;

Db 20 EVQVSEGGGLVPGGSLKLSCAASGFAFSYAMSVROSPEKRLWVAEISSGGNYAY 79
QY 1 EVQVSEGGGLVPGGSLKLSCAASGFAFSYDMSWVRQTPKRLWVAYISSGGTTY 60
Db 80 QDVTGRTISRDNKNTLYLQMSLSKASEDTAMTYCARHSGYGVLFAYWGQGLT 136
QY 121 VSA 123
```



DR WPI: 98-230640/20.  
 PT New chimeric antibodies against human parathormone related peptide(s) - useful for, e.g. treatment of hypercalcaemia and other disorders caused by malignant neoplasm(s)  
 PS Claim 5; Page 111-112; 182pp; Japanese.  
 CC New antibodies have been developed which are specific for human parathormone related peptides (hPTHrP). The antibodies comprise chimeric L and/or H chains, where the C region is of human and L region of mouse, origin. The present sequence represents a specifically claimed region of an antibody of the invention. Host cells, transformed with vectors containing DNA encoding antibodies of the invention, can be used to produce the antibodies. The antibodies may be used to treat hypercalcaemia, especially that due to a malignancy, e.g. cancers of pancreas, lung, throat, larynx, tongue, gum, oesophagus, stomach, liver, breast, kidney, bladder, womb or prostate or malignant lymphoma. They may also be used for treatment of hypophosphatemia such as that due to pathogens or to vitamin D resistance.  
 CC Sequence 118 AA;  
 SQ  
 Query Match 79.3%; Score 716; DB 1; Length 118;  
 Best Local Similarity 82.9%; Pred. No. 1.74e-48;  
 Matches 102; Conservative 9; Mismatches 7; Indels 5; Gaps 2;  
 Db 1 EVQVLESAGDLVKKPGSILKSCAAGFTFFSSYGMWIRTPDKRLWVATISSGSGTYTY 60  
 QY 1 EVQVLESAGDLVKKPGSILKSCAAGFTFFSSYGMWIRTPDKRLWVATISSGSGTYTY 60  
 Db 61 PDVAVGRTFISDNKNTLYLQMSLSKSEDTAMFYCARQTT--MTY---FAYWGCTLYT 115  
 QY 61 PDVAVGRTFISDNKNTLYLQMSLSKSEDTAMFYCARHSGSGSYGVLFAYWGCTLYT 120  
 Db 116 VSA 118  
 QY 121 VSA 123  
 RESULT 12  
 ID W89625 standard; protein; 137 AA.  
 AC W89625;  
 DT 14-APR-1999 (first entry)  
 DE Mouse humanised antibody #23-57-137-1 heavy chain protein.  
 KM Human; parathyroid hormone related protein; PTHrP; cachexia; cancer;  
 OS Mus sp.  
 OS Synthetic.  
 OS Key  
 FT Peptide Location/Qualifiers  
 FT 1-19  
 FT /label= signal  
 FT 20.137  
 PT Protein  
 PN W09851329-A1.  
 PD 19-NOV-1998.  
 PE 13-MAY-1998; J02116.  
 PR 18-JUL-1997; JP-194445.  
 PR 15-MAY-1997; JP-125505.  
 PA (CHUS ) CHUGAI SEIYAKU KK.  
 PI Ishii K, Sato K, Tsumenari T;  
 DR WPI: 99-070101/06.  
 DR N-PSDB: X00092.  
 PT Inhibitors of binding of parathyroid hormone related peptide to its receptor - useful for, e.g. treatment of cachexia arising from cancer or other diseases  
 PS Example 2; Page 82; 125pp; Japanese.  
 CC The present invention describes compositions for the treatment of cachexia containing a substance which inhibits the binding of a parathyroid hormone related peptide (PTHrP) to its receptor, as an active component. This substance may be an antagonist to the receptor, or an antibody (preferably monoclonal) or antibody fragment, recognising PTHrP. The antibody is preferably humanised or chimeric. The present invention also describes a humanised antibody prepared by hybridoma 23-57-137-1 (FERM BP-5631). The composition is used for the treatment of cachexia arising in connection with diseases such as cancer, thereby improving the quality of life of the patient. The present sequence represents mouse humanised antibody heavy chain from

CC #23-57-137-1 from the present invention.  
 SQ Sequence 137 AA;  
 Query Match 79.3%; Score 716; DB 1; Length 137;  
 Best Local Similarity 82.9%; Pred. No. 1.74e-48;  
 Matches 102; Conservative 9; Mismatches 7; Indels 5; Gaps 2;  
 Db 20 EVQVLESAGDLVKKPGSILKSCAAGFTFFSSYGMWIRTPDKRLWVATISSGSGTYTY 79  
 QY 1 EVQVLESAGDLVKKPGSILKSCAAGFTFFSSYGMWIRTPDKRLWVATISSGSGTYTY 60  
 Db 80 PDVAVGRTFISDNKNTLYLQMSLSKSEDTAMFYCARQTT--MTY---FAYWGCTLYT 134  
 QY 61 PDVAVGRTFISDNKNTLYLQMSLSKSEDTAMFYCARHSGSGSYGVLFAYWGCTLYT 120  
 Db 135 VSA 137  
 QY 121 VSA 123  
 RESULT 13  
 ID W57592 standard; protein; 137 AA.  
 AC W57592;  
 DT 03-SEP-1998 (first entry)  
 DE Chimeric antibody against hPTHrP H chain V region SEQ ID NO:57.  
 KM Chimeric; antibody; human parathormone related peptide; hPTHrP; mouse; L chain; H chain; hypercalcaemia; cancer; malignant lymphoma; CDR; hypophosphatemia; pathogen; vitamin D resistance; V region; C region; humanised.  
 OS Synthetic.  
 OS Chimeric - Mus sp.  
 OS Chimeric - Homo sapiens.  
 PN W09813388-A1.  
 PD 02-APR-1998.  
 PE 24-SEP-1997; J03382.  
 PR 24-JUL-1997; JP-214168.  
 PR 26-SEP-1996; JP-255196.  
 PA (CHUS ) CHUGAI SEIYAKU KK.  
 PI Sato K, Wakanara Y, Yabuta N;  
 DR WPI: 98-230640/20.  
 DR N-PSDB: V24232.  
 PT New chimeric antibodies against human parathormone related peptide(s) - useful for, e.g. treatment of hypercalcaemia and other disorders caused by malignant neoplasm(s)  
 PS Claim 52; Page 120-121; 182pp; Japanese.  
 CC New antibodies have been developed which are specific for human parathormone related peptides (hPTHrP). The antibodies comprise chimeric L and/or H chains, where the C region is of human and L region of mouse, origin. The present sequence represents a specifically claimed region of an antibody of the invention. Host cells, transformed with vectors containing DNA encoding antibodies of the invention, can be used to produce the antibodies. The antibodies may be used to treat hypercalcaemia, especially that due to a malignancy, e.g. cancers of pancreas, lung, throat, larynx, tongue, gum, oesophagus, stomach, liver, breast, kidney, bladder, womb or prostate or malignant lymphoma. They may also be used for treatment of hypophosphatemia such as that due to pathogens or to vitamin D resistance.  
 CC Sequence 137 AA;  
 SQ  
 Query Match 79.3%; Score 716; DB 1; Length 137;  
 Best Local Similarity 82.9%; Pred. No. 1.74e-48;  
 Matches 102; Conservative 9; Mismatches 7; Indels 5; Gaps 2;  
 Db 20 EVQVLESAGDLVKKPGSILKSCAAGFTFFSSYGMWIRTPDKRLWVATISSGSGTYTY 79  
 QY 1 EVQVLESAGDLVKKPGSILKSCAAGFTFFSSYGMWIRTPDKRLWVATISSGSGTYTY 60  
 Db 80 PDVAVGRTFISDNKNTLYLQMSLSKSEDTAMFYCARQTT--MTY---FAYWGCTLYT 134  
 QY 61 PDVAVGRTFISDNKNTLYLQMSLSKSEDTAMFYCARHSGSGSYGVLFAYWGCTLYT 120  
 Db 135 VSA 137  
 QY 121 VSA 123

QY 121 VSA 123

## RESULT 14

ID W11917 standard; Protein; 247 AA.  
AC W11917;  
DE 24-JUN-1997 (first entry)  
DE Murine MAB SK48-E26 heavy chain.  
KW Interleukin-1 beta; IL-1 beta; recombinant antibody;  
KW humanised antibody; chimeric antibody; antibody engineering;  
KW monoclonal antibody; MAB; SK48-E26; inflammation; therapy.  
OS Homo sapiens.  
FH key Location/Qualifiers  
FT peptide 1..19  
FT /label= Sig\_peptide  
FT region 20..49  
FT /label= FR1  
FT /note= "framework region 1"  
FT region 50..54  
FT /label= CDR1  
FT /note= "complementarity determining region 1  
(Claim 10, page 48)"  
FT region 55..68  
FT /label= FR2  
FT /note= "framework region 2"  
FT region 69..85  
FT /label= CDR2  
FT /note= "complementarity determining region 2  
(Claim 10, page 48)"  
FT region 86..117  
FT /label= FR3  
FT /note= "framework region 3"  
FT region 118..127  
FT /label= CDR3  
FT /note= "complementarity determining region 3  
(Claim 10, page 48)"  
FT region 128..138  
FT /label= FR4  
FT /note= "framework region 4"  
FT region 139..247  
FT /label= Constant\_region  
WO9501997-A1.  
19-JAN-1995.  
PF 07-JUL-1994; U07659.  
PR 09-JUL-1993; US-090534.  
PR 04-MAR-1994; US-206190.  
PA (SMIK ) SMITHKLINE BEECHAM CORP.  
PI Gross MS, Hurler MR, Jackson JR, Jonak ZL, Theisen TW;  
PI Young PR;  
DR WPI; 95-066868/09.  
DR N-PSDB; T51436.  
PT Recombinant and humanised chimeric antibodies against human  
PT interleukin-1-beta - for preventing and treating  
PT interleukin-mediated inflammatory disorders  
PS Claim 5; Page 36-37; 62pp; English.  
CC Amino acid sequences of the heavy chain (W11917) and light chain  
CC (W11918) of anti-human interleukin-1 beta (IL-1 beta) murine  
CC monoclonal antibody (MAB) SK48-E26 were deduced from nucleic acids  
CC (T51436-37) derived from hybridoma SK48-E26. The heavy and light  
CC chains, esp. the complementarity determining region sequences,  
CC can be utilised in novel recombinant chimeric and humanised  
CC antibodies (see also W11919-20) useful for the treatment and  
CC prevention of IL-1 mediated inflammatory disorders.  
SQ Sequence 247 AA;

Query Match 79.3%; Score 716; DB 1; Length 247;

Best Local Similarity 84.6%; Pred. No. 1.74e-48;

Matches 104; Conservative 5; Mismatches 10; Indels 4; Gaps 2;

Db 20 EVHVESGGGLVLPKGGSLKLSCAASGFAFSYDMSWVRQTPKRLDWAYISSGGGTTY 79

QY 1 EVQLVESGGGLVLPKGGSLKLSCAASGFAFSYDMSWVRQTPKRLDWAYISSGGGTTY 60

Db 80 PDTVKGRTISRDNKNTLYLQMSLSKSDTAMYCARHSGYGVLFAYWGQGLT 135  
QY 61 PDTVKGRTISRDNKNTLYLQMSLSKSDTAMYCARHSGYGVLFAYWGQGLT 120

Db 136 VSS 138

QY 121 VSA 123

## RESULT 15

ID W86122 standard; Protein; 121 AA.  
AC W86122;  
DE 03-MAR-1999 (first entry)  
DE Protein sequence of de-immunised 340 Vh.  
KW Non-immunogenic; epitope; T-cell; immunogenicity; immune system; SK;  
KW immunoglobulin; therapeutic; streptokinase; de-immunised.  
OS Homo sapiens.  
PN WO9852976-A1.  
PD 26-NOV-1998.  
PF 21-MAY-1998; G01473.  
PR 14-APR-1998; GB-007751.  
PR 21-MAY-1997; GB-010480.  
PR 31-JUL-1997; GB-016197.  
PR 28-NOV-1997; GB-025270.  
PR 02-DEC-1997; US-067235.  
PA (BIOV-) BIOVATION LTD.  
PI Carr FJ;  
DR WPI; 99-045301/04.  
PT Reducing immunogenicity of proteins - by modifying the amino acid  
PT sequence of the protein to eliminate potential epitopes for T-cells  
PT of a given species  
PS Example 1; Fig 5; 77pp; English.  
CC The invention relates to a method for the production of non-immunogenic  
CC proteins. The method comprises determining at least part of the amino  
CC acid sequence of the protein; (b) identifying in the amino acid sequence  
CC one or more potential epitopes for T-cells (T-cell epitopes) of the given  
CC species; and (c) modifying the amino acid sequence to eliminate at least  
CC one of the T-cell epitopes identified in step (b) thereby to eliminate or  
CC reduce the immunogenicity of the protein when exposed to the immune  
CC system of the given species. A method of analysing a pre-existing protein  
CC to predict the basis for immunogenic responses is also provided. The  
CC methods can be used particularly for reducing the immunogenicity of  
CC immunoglobulins or therapeutic proteins, e.g. Streptokinase (SK). The  
CC products can be used for diagnosis and therapy. The present sequence  
CC represents the protein sequence of de-immunised 340 Vh.  
SQ Sequence 121 AA;

Query Match 79.0%; Score 713; DB 1; Length 121;

Best Local Similarity 78.9%; Pred. No. 3.10e-48;

Matches 97; Conservative 10; Mismatches 14; Indels 2; Gaps 1;

Db 1 EVQLVESGGGLVLPKGGSLKLSCAASGFTDTYDMSWVRQAPKGLWVAYIGSGGDTTY 60

QY 1 EVQLVESGGGLVLPKGGSLKLSCAASGFAFSYDMSWVRQTPKRLDWAYISSGGGTTY 60

Db 61 PDTVKGRTISRDNKNTLYLQMSLSKSDTAMYCARHSGYGVLFAYWGQGLT 118

QY 61 PDTVKGRTISRDNKNTLYLQMSLSKSDTAMYCARHSGYGVLFAYWGQGLT 120

Db 119 VSS 121

QY 121 VSA 123

Search completed: Mon Oct 2 09:33:25 2000

Job time : 14 secs.



US-09-381-49

Query Match 97.0%; Score 734; DB 1; Length 131;  
Best Local Similarity 97.2%; Pred. NO. 9.32e-50;  
Matches 104; Conservative 2; Mismatches 1; Indels 0; Gaps 0;

Db 21 DIQMTQTSSLSASLGDRVTISCRASQDISNYLNWYQOKPDGTVKLLIYYTSSLRHSGVPS 80  
 Qy 1 DIQMTQTSSLSASLGDRVTISCRASQDISNYLNWYQOKPDGTVKLLIYYTSSLRHSGVPS 60  
 Db 81 RFSGSGSGTDYSLTISNLEQEDIATYFCQQNGTLPWTFGGGKTGLEIK 127  
 Qy 61 RFSGSGSGTDYSLTISNLEQEDFATYFCQQNGTLPWTFGGGKTGLEIK 107